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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,507	02/28/2002	Donald G. Munroe	108074-00023	8368
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ROTHWELL, FIGG, ERNST & MANBECK, P.C. 1425 K STREET, N.W. SUITE 800 WASHINGTON, DC 20005				
			EXAMINER DEBERRY, REGINA M	
			ART UNIT 1647	PAPER NUMBER

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/084,507

Applicant(s)

MUNROE ET AL.

Examiner

Regina M. DeBerry

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 44-51 and 53-64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 44-51 and 53-64 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Status of Application, Amendments and/or Claims

The amendment filed 25 August 2004 has been entered in full. Claims 1-43 and 52 were cancelled. New claims 60-64 were added. Claims 44-51, 53-64 are under examination.

The specification is in compliance with 37 CFR 1.821-1.825 of the Sequence Rules and Regulations.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection to claims 44-52 under 35 U.S.C. 112, second paragraph, as set forth at page 8 of the previous Office Action (25 February 2004) is *withdrawn* in view of the amendment (25 August 2004).

The rejection to claims 44-51 under 35 U.S.C. 102(b) as being anticipated by Hecht *et al.* (The Journal of Cell Biology, Vol.135/4 November, 1996), as set forth at pages 9-10 of the previous Office Action (25 February 2004) is *withdrawn* in view of the amendment (25 August 2004).

Specification Objection

The amendment filed 17 December 2003 remains objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: wherein the

response measured in step (c) is selected from GTP γ S binding (claims 55 and 60).

The basis for this rejection is set forth at page 3 of the previous Office Action (25 February 2004). Applicant combines the arguments against the specification objection and 35 U.S.C. 112, first paragraph, written description, new matter rejection.

Applicant's arguments have been fully considered but not deemed persuasive. Please see the maintained 35 U.S.C. 112, first paragraph, written description, new matter rejection below.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description, New Matter

Claims 55 and 60 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This was a new matter rejection. The basis for this rejection is set forth at pages 3-4 of the previous Office Action (25 February 2004).

Applicant states that with respect to GTP γ S, that it is generally known in the field of signal transduction that activation through G-protein coupled receptors requires signaling through G-protein. Applicant argues that it is known that G-protein signaling of such receptors requires GTP binding. Applicant submits that disclosing that the EDG is such a G-protein coupled receptor provides sufficient support for those of skill in the art to understand that measuring GTP γ S binding indicates whether the tested material is an agonist or antagonist of the receptor using the assays as described in the disclosure.

Applicant's arguments have been fully considered but not deemed persuasive. The Examiner understands that signal transduction occurs through the activation of

G-protein coupled receptors and requires GTP binding. However, the instant claims are drawn to *methods for measuring a response indicative of the degree of an agonist activity by specifically measuring GTP γ S binding*. The claims encompass assays/experiments to measure GTP binding. The specification, as originally filed, does not provide support for the invention as now claimed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

Claims 44-51 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of identifying a compound as an agonist for *EDG-2, EDG-3, EDG-4, EDG-5 and EDG-6 receptors* using the readout of an NF- κ B assay OR

a method of identifying a compound as an antagonist for *EDG-2, EDG-3, EDG-4, EDG-5 and EDG-6 receptors* using the readout of an NF- κ B assay and

a method of identifying a compound as an agonist for *EDG-4 receptor* using the readout of an IL-8 assay OR

a method of identifying a compound as an antagonist for *EDG-4 receptor* using the readout of an IL-8 assay

does not reasonably provide enablement for:

a method of identifying a compound as an agonist for all *EDG receptors* or a method of identifying a compound as an antagonist for all *EDG receptors* using the readouts of NF- κ B and/or IL-8 assays. The basis for this rejection is set forth at pages 5-6 of the previous Office Action (25 February 2004).

Applicant argues that claims 44-51 as amended are directed to a method of determining whether a compound is an agonist or antagonist for an EDG receptor, which activate NF- κ B and/or produce IL-8. Applicant argues that the disclosure specifically recites methods and assays for determining agonist and antagonist activity by for example measuring IL-8 production or NF- κ B activation in Examples 1 and 11, in addition to the Examples 14-19.

Applicant's arguments have been fully considered and are deemed partly persuasive. The Examiner agrees with Applicant that the specification teaches NF- κ B activation and IL-8 production in the presences of **some EDG receptors**. However, as was stated in the last Office Action, the specification teaches IL-8 production only in the presence of activated EDG-4 receptor (page 35, lines 25-28 and page 37, lines 18-25). The specification teaches that NF- κ B was not activated/induced in the presence of activated EDG-1 receptor (page 45, lines 5-10). Thus, the instant specification teaches that the recited assays cannot be used to determine agonist/antagonist activity for all types of EDG receptors. The claims, as amended, still encompass readouts/assays for all varieties of EDG receptors.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 53-64 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The basis for this rejection is set forth at pages 6-7 of the previous Office Action (25 February 2004).

Applicant directs the Examiner's attention to Example 10A on page 35 of the specification with respect to the rejection based on measuring the modulation of cellular cyclic AMP levels. Applicant argues that such assays are disclosed.

Applicant's arguments have been fully considered but not deemed persuasive. The instant claims are drawn to a method of measuring a response *indicative of the degree of an agonist or an antagonist activity, wherein the response measures the modulation of cellular cyclic AMP levels*. Applicant cites Example 10A, page 35, which states, "We used a cAMP inhibition assay to show the presence of functional S1P receptors in Swiss 3T3, mouse neuronal B-103 and hamster CHO Pro5 cells". "By comparing the cAMP responses of these cells to the expression profile of the 7 identified edg receptors, we speculated that both EDG-3 and EDG-4 are likely to be S1P receptors". The specification fails to teach if cAMP inhibition is indicative of agonist or antagonist activity. The specification fails to teach if modulation of cellular cyclic AMP levels mean increase or decrease? The specification fails to disclose a protocol and the proper parameters/controls when employing these experiments. The specification fails to teach how to identify a compound as an agonist or antagonist of an EDG receptor wherein the agonist or antagonist activity is measured by modulation of cellular cyclic AMP levels.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 112, Second Paragraph

Claims 46, 53-64 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The basis for this rejection is set forth at pages 8-9 of the previous Office Action (25 February 2004).

Applicant states that claim 53, as amended, is directed to measuring an agonist response and claim 54 to measuring an antagonist response. Applicant argues that this amendment make the rejections with respect to whether an increase or a decrease is measured in claims 55 and 57 moot, as agonist activity results in an increase in receptor response whereas antagonist activity (in claims 54 and 60-64) results in a decrease or inhibition of receptor response.

Applicant's arguments have been fully considered but not deemed persuasive. "Measuring a response indicative of the degree of an agonist activity" (claim 53) and "measuring a response indicative of the degree of an antagonist activity" (claim 54) is indefinite because it is not clear exactly what response is being measured. The metes and bounds of claims 53 and 54 cannot be determined because the claims do not recite any assays and/or responses to discern agonist and/or antagonist activity.

Applicant states, "agonist activity results in an increase in receptor response whereas antagonists activity (in claims 54 and 60-64) results in a decrease or inhibition of receptor response". Yet, the responses for identifying a compound as an agonist and

identifying a compound as an antagonist are the same (compare claims 55-59 with claims 60-64). Thus, it is unclear how to discern the difference between agonists and antagonists of SEQ ID NO:17 and SEQ ID NO:22.

Claims 55 and 60 remain indefinite because it is unclear if "modulation of cellular cyclic AMP levels" means increase or decrease and because the claims recite improper Markush groups.

The scientific reasoning and evidence as a whole indicates that the rejections should be maintained.

New claim objection: Claim 46 is objected to because IL-8 is misspelled (IL-8 instead of IL-8).

Conclusion


No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


RMD
11/2/04

Elizabeth C. Kemmerer

ELIZABETH C. KEMMERER
PATENT EXAMINER